whether the induction of proliferative arrest in SAMs by fruit/seed-produced auxin might involve similar mechanisms as arrest in the dormant axillary buds induced by apically produced auxin in apical dominance. The dormant axillary buds were proposed to result partly from auxin-mediated inhibition of CK biosynthesis in the stem or from reduced auxin export from the axillary bud[5,15]. These potential mechanisms could be tested in arrested meristems by analyzing CK signaling and biosynthesis pathway mutants and their genetic interactions with fruit/seed-pathway mutants, including those with defects in auxin biosynthesis and transport. Additionally, since fruit/seed-derived auxin only causes proliferative arrest in older SAMs[5], how the age-dependent pathway confers competence to arrest is another important question. Finally, as monocarpy has evolved several times from polycarpy, there may be species-specific regulatory mechanisms[2]. Comparative analyses of the end of flowering in different monocarpic species will illuminate strategies that balance growth with reproduction.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Infectious disease: Dog diets may drive transmission cycles in human Guinea worm disease

Robert L. Richards[1,*] and Lauren A. Holian[1,2]
[1]Department of Biology, Louisiana State University, Baton Rouge, LA 70803, USA
[2]Department of Biological Sciences, University of South Carolina, Columbia, SC 29208, USA
*Correspondence: robbielrichards@gmail.com
https://doi.org/10.1016/j.cub.2022.01.005

Domestic dogs have an important role in the ecology of transmission of the Guinea worm, a debilitating human parasite. A new study documents how fish content in dogs' diets can predict Guinea worm infection status, suggesting additional avenues for control.

In the early 2000s, Guinea worm (*Dracunculus medinensis*) seemed poised to become the second human infectious disease ever eradicated, after smallpox (Variola sp.). Prior to eradication initiatives, Guinea worm caused painful and debilitating infections in millions of people annually and, like smallpox, had no known animal reservoir, making it a prime candidate for the next eradication[1,2]. Guinea worm eradication initiatives found much success, resulting in the number of endemic countries shrinking to a handful by the early 2010s[1]. It was at this point,

however, that Guinea worm-like infections were first noticed in domestic dogs along the River Chari in the Republic of Chad[3] (Figure 1). Over the subsequent decade, Guinea worm was increasingly detected in dogs, and it became clear that transmission between dogs and humans had become a substantial barrier to eradication[3,4]. Although public health workers have attempted to interrupt dog transmission using a range of interventions, much remains unknown about the ecology of the parasite in this newly discovered host[3]. A new study by Cecily E.D. Goodwin and colleagues[5] published in this issue of *Current Biology* reports a combination of GPS tracking and repeated, temporally resolved, stable-isotope diet analyses to identify the relationship between Guinea worm cases in domestic dogs and both proximity to water sources and fish in their diets.

D. medinensis follows a peculiar life cycle, making cases difficult to predict but transmission straightforward to interrupt, at least in theory. Larval worms floating in freshwater are ingested by and infect aquatic invertebrates (copepods). These copepods are subsequently ingested by humans in drinking water, allowing the worm to escape the digested copepod and migrate to human subcutaneous tissues, typically on the foot or lower leg. After a 10–14 month-long developmental period, a blister forms on the host's skin which, when exposed to water, bursts and discharges larvae into the water, completing the cycle[1,6]. The blister is extremely painful and without careful extraction of the worm it can become seriously infected[6]. Due to this peculiar life cycle, eradication initiatives focused primarily on three interventions: identifying infectious blisters prior to worm emergence and preventing discharge into drinking water, treating water sources to kill copepods, and filtering water before drinking to exclude infected copepods[1]. These initiatives have been extremely successful, resulting in fewer than 30 human cases globally in 2020[7]. The discovery of Guinea worm in domestic dogs has, however, substantially complicated the path to eradication. In fact, given the relative numbers of cases, it now seems likely that domestic dogs in Chad are primarily responsible for maintenance of the parasite, and human cases are the result of spillover (or really 'spillback') events[3]. The populations of *D. medinensis* in humans and dogs are genetically indistinguishable, further reinforcing the key role of dogs in the persistence of Guinea worm in humans[8].

Figure 1. Guinea worm in domestic dogs.
(A) Free-ranging domestic dogs (*Canis lupus familiaris*) are common in rural areas of Chad. (B) Guinea worm (*Dracunculus medinensis*) prevalence is typically high in these dog populations, erupting painfully from the feet and shedding larvae into water sources. (C) Although it is possible that dogs become infected through their drinking water, access to raw fish and fish entrails has been implicated as a potentially important alternative mode of transmission. (Photo: Jared Wilson-Aggarwal.)

Dogs and their worms

Since Guinea worm was detected in domestic dogs, public health initiatives have implemented interventions to interrupt dog transmission while researchers studied the ecology of the parasite in dogs. Eradication efforts have focused on applying the lessons learned in humans to dogs, including provisioning of clean water and tethering dogs suspected of infection[3,7,9]. Research has emphasized the importance of understanding how and why dogs are infected. Large-scale observational studies identified broad correlates of dog infection including the importance of water proximity and conflicting findings on the effect of water provisioning and whether villages were primarily composed of fishers[9–12]. Other researchers have focused, instead, on understanding the mechanisms by which dogs become infected. Notably, the key route of human infection (drinking contaminated water) may not apply to dogs. Whereas we scoop large volumes of water for drinking, dogs lap at the surface of water sources. As a result, infected copepods that are incidentally captured and consumed by human drinking practices are much more likely to flee from and escape the lapping tongue of a dog[13].

The primary mechanism for dog infection has therefore become a key question for parasitologists, ecologists, and public health practitioners. Researchers have identified dog ingestion of uncooked frogs and fish as potential alternative routes for transmission of *D. medinensis*[14–16]. The worm has been found both encysted in frog tissue and alive within copepods in the guts of fish[15,16]. Fish guts are a particularly appealing transmission mechanism due to the extensive fishing practices along the River Chari in Chad (where the majority of global dog cases occur) and the access of domestic dogs to raw fish scraps from their owners[7,11,12,15]. However, researchers have struggled to directly associate fish consumption by dogs with Guinea worm infection risk in the field.

Taking a closer look at dog behavior

In the new study, Goodwin *et al.*[5] investigated the ecological plausibility of fish as a route of infection for dogs in Chad, where 97.4% of all Guinea worm infections reported in 2020 were detected.

They followed cohorts of adult dogs across six villages along the River Chari, where the prevalence of Guinea worm in dogs is known to be high. They were able to track the movements and diets of 72–91% of the domestic dogs throughout the year with sampling bouts representing each climatic season. Dog movements were tracked (10-minute intervals for 2–6 weeks) and compared to satellite imagery of local water sources. Diet composition was determined through comparative stable isotope analysis of dog's whiskers throughout the year and samples of local food resources that dogs may be accessing. Despite the limited timing of whisker samples, an impressive monthly temporal resolution of diet was achieved by segmenting samples according to whisker growth rates and analyzing segments individually.

To elucidate whether a novel transmission route is plausible, the movement and diet data were then considered in the context of each dog's history of Guinea worm disease. Specifically, the authors collected records of whether each dog had been observed with a worm emergence between 2016–2018 and the worm emergence rate (number of observed months with a worm emergence).

In the hot-dry season, when worm emergence rates were highest, dogs with more fish in their diet and which spent more time around ponds had higher Guinea worm emergence. In the wet season, emergence was only positively associated with fish consumption and there was no relationship with either variable in the cool-dry season. Between dogs, variability in fish consumption was best explained by physical characteristics, sampling season, region, and the household's distance from the River Chari. Collinearities between fish consumption and proximity to water made the interpretation of these results challenging, but the authors used a combination of model comparison and expert knowledge to suggest that the role of fish consumption acts as more than just a proxy for proximity to water.

Answers and new questions

The relationship between pond proximity and Guinea worm emergence suggests that recent initiatives to tether dogs away from water may prove effective. If, however, tethered dogs still have access to fresh caught fish and fish scraps, fully interrupting transmission through tethering may be difficult. Recent initiatives that involve burning or burying fish scraps and limiting dog access, alongside tethering, should prove fruitful. Indeed, recent trends suggest that they are effective. Since 2017 >80% of households in at-risk communities were burying fish entrails and >80% of infected dogs were tethered in 2020[7]. At the same time, the first half of 2021 showed a 60% decrease in infected dogs compared to the same period in 2020[7]. Although it is difficult to identify the specific drivers of the decrease, the work of Goodwin *et al.*[5] is highly suggestive that dog diets play a key role. Goodwin *et al.*[5] martialed methods spanning behavioral ecology, telemetry, landscape mapping, diet analysis, and structured surveys to provide clear additional evidence for the relationship between fish-based diets and Guinea worm in dogs. These findings will help public health professionals continue to develop a new roadmap towards control and eradication in the presence of dog hosts. But they also raise additional questions that will require an even wider range of methods and disciplines to address: Are other fish-eating mammals likely hosts of Guinea worm (we know that a few are!)[17]? Are public health efforts to limit fish access by dogs actually decreasing infection rates? Is limiting dog infection or limiting onward transmission by dogs more effective at preventing human infection? Which is more sustainable for Chadians long-term? Will extended periods of tethering and limiting fish access even be sufficient to eradicate Guinea worm in dogs in Chad?

Beyond its direct utility to eradication efforts, this study highlights a key lesson to be learned from Guinea worm: parasites jumping from humans to other animals before jumping back (known as spillback) poses a real threat to disease-control efforts. Because the ecology of transmission in new populations may differ wildly from transmission ecology in humans, a holistic understanding of the relevant ecosystem(s) becomes essential. Such circumstances require the creative application of methods from diverse fields in order to adapt to a changing disease landscape.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Glycemic control: Tanycytes march to the beat of the suprachiasmatic drummer

Monica Imbernon, Benedicte Dehouck, and Vincent Prevot*
Inserm, CHU Lille, Laboratory of Development and Plasticity of the Neuroendocrine Brain, Lille Neuroscience and Cognition, University of Lille, UMR-S1172, EGID, Lille, France
*Correspondence: vincent.prevot@inserm.fr
https://doi.org/10.1016/j.cub.2022.01.038

The suprachiasmatic nucleus (SCN) synchronizes physiology with the individual's environment to optimize bodily functions. A new study reveals that tanycytes follow the tempo set by the SCN to effect circadian changes in both brain entry of blood glucose and glycemia.

Circadian rhythms are orchestrated in the hypothalamus by the suprachiasmatic nucleus (SCN), which acts as a central clock sending time-controlled information to many different brain areas via synaptic transmission. This temporal information regulates hormonal and autonomic output in order to synchronize body functions to the light/dark cycle, thus ensuring that the organism can operate optimally within its environment[1]. For example, while circulating glucose levels at a given time of day are strictly maintained with very little variation, over the circadian cycle, basal glucose concentrations, when expressed as a percentage of the 24 h mean, can undergo a doubling[2]. The SCN lowers body temperature and glucose levels at the start of the sleep phase, but raises them during the active phase to support increased energy consumption. However, the exact mechanism by which the SCN influences other hypothalamic networks to control these variations across time remains unknown. In a study reported in this issue of *Current Biology*, Rodríguez-Cortés, Hurtado-Alvarado *et al.*[3] used site-specific brain lesions and neuroanatomical, physiological, and pharmacological approaches to investigate how the SCN communicates with tanycytes to allow circulating glucose to periodically access glucose-sensing neurons in the arcuate nucleus of the hypothalamus (ARH) and thus regulate circadian changes in glycemia.

The ARH lies adjacent to the median eminence (ME), a circumventricular organ controlling the access of blood-borne molecules. These molecules provide essential information to ARH neurons that regulate feeding and thus prompt adaptive changes to maintain energy homeostasis[4]. The ME forms the floor of the third ventricle in the tuberal region of the hypothalamus and is irrigated by the underlying pituitary portal capillary plexus, characterized by a fenestrated endothelium and high permeability to circulating hormones and nutrients[4]. The cytoarchitecture of the ME is shaped by specialized ependymoglial cells called tanycytes whose cell bodies line the third ventricle and send long, slender processes that terminate in end-feet. These feet contact the vascular walls of either the pituitary portal vessels or parenchymal vessels with a normal endothelium and tight junctions between endothelial cells that constitutes the blood–brain barrier[4]. The free diffusion of blood-borne molecules extravasating from the fenestrated vessels into the cerebrospinal fluid (CSF) is prevented by organized tight-junction complexes that circle tanycytic cell bodies and seal the paracellular space[5].

Importantly, tanycytes are also able to sense minute changes in energy status and modulate the parenchymal area directly accessible to blood-borne molecules by controlling the